AF 1642

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In Re Appln. of:	Eugene Roussel	Group Art Unit:	1642
Serial No.:	09/756,978	Conf. No.:	6809
Filed:	9 January 2001	Examiner:	Misook Yu
For:	Therapeutic Modulation of the Tumor Inflammatory Response	Atty Docket No.:	E0631-00001

APPLICANT'S INTERVIEW SUMMARY

This Summary is filed to comply with the Applicant's responsibility, pursuant to 37 C.F.R. §1.133(b) to provide a complete written statement of the reasoning presented during the telephone interview conducted on 3 June 2004 with respect to the patent application referenced above.

On 3 June 2004, Applicant Eugene Roussel, his representative, Gary D. Colby, and Russell Timm (an employee of the firm representing Applicant Roussel) conducted a personal interview with Examiners Misook Yu, Christina Chan, and Anthony Caputa, beginning shortly after 10:00 a.m. The interview continued until shortly after 11:00 a.m.

Exhibits and Demonstrations

The exhibits presented during the 18 May 2004 interview were referred to.

A simple diagram composed of a circle (representing a tumor site) and several crosses (representing leukocytes), some located within the circle and others located outside the circle, was made by Examiner Yu and referred to during discussions and was retained (if at all) by the examiners. To the best of the Applicant's recollection, that diagram also included several radially-disposed arrows extending from without the circle toward the circle.

A Draft Amendment and Request for Reconsideration guided the Applicant's comments during the interview. A copy of the Draft Amendment which had been previously

faxed to Examiner Yu was left with the Examiners. The Applicant believes that the Draft Amendment was attached to the Examiner's Interview Summary sheet in the file wrapper.

Claims Discussed

Rejections pertaining to all claims were discussed.

Prior Art Discussed

The Lee, Tannenbaum, and Lanni references (of record) referred to in Paper No. 27 were discussed. A four-page excerpt from Parslow (subsequently submitted with an Amendment and Request for Reconsideration submitted by fax on 3 June 2004) was briefly discussed. No other specific prior art was discussed substantively.

Proposed Amendments

No amendments to the claims or the specification were discussed during the interview.

Principal Arguments Presented

The Applicant briefly reviewed that all of the claims recite local administration to a tumor in a human of:

1. An antigen-releasing agent
2. A leukocyte attractant
3. IFN-g and
4. A second type 1 inflammatory response- (IR1-)promoting agent.

The discussions during the interview largely centered around the obviousness rejection of most claims over Lee in view of Tannenbaum and/or Lanni. The Applicant presented the arguments set forth in the Draft Amendment.

With regard to the Applicant's allegation that anti-Fas antibodies were inappropriate for use as the "antigen-releasing agent" recited in the claims, the Applicant

clarified that at least most leukocytes, including all activated T lymphocytes, express Fas protein on the cell surface. Thus, local administration of anti-Fas antibody to a tumor in an animal (as disclosed in Lee) would be expected by a skilled artisan to kill lymphocytes that exist or arrive at the tumor site.

In response to questioning by the Examiners, the Applicant pointed out that the RENCA tumor cells used by Lee et al. were not killed by anti-Fas antibodies unless they were engineered to express Fas at a relatively high level. The Applicant indicated that it could not be ruled out that some tumors might naturally express Fas protein at a sufficiently high level that they would be expected to be killed by contact with anti-Fas antibodies. Nonetheless, the Applicant pointed out that because the interaction between Fas protein on leukocytes and FasL (the naturally-occurring ligand of Fas - analogous to anti-Fas antibodies in the context of the rejection) is disclosed in the Parslow et al. excerpt to be involved in clonal selection of leukocytes, the skilled artisan would expect that anti-Fas antibodies would kill substantially any Fas-bearing leukocyte.

The Examiners suggested that if anti-Fas antibodies could be expected to kill at least certain tumors (i.e., those that express Fas at high levels), then anti-Fas antibodies might be an effective anti-tumor agent, regardless of potential effects on leukocytes. The Applicant replied that, regardless of any anti-tumor efficacy of anti-Fas antibodies, a skilled artisan would recognize the leukocyte-killing effects of those antibodies, and would have no motivation to locally administer to the tumor the other components recited in the claims (i.e., the leukocyte attractant, IFN-g, and second IR1-promoting agent), since those agents act on the leukocytes, rather than on the tumor cell.

The Applicant pointed out that Lee does not disclose administering IFN-g or TNF (a second IR1-promoting agent) to a tumor in any animal. In Lee, those compounds were used solely to mimic *in vivo* levels of the compounds in *in vitro* experiments. In fact, one of the conclusions of Lee was that endogenous levels of IFN-g production were required in order to observe the apoptosis-inducing effect of anti-Fas antibodies on Fas-overexpressing RENCA cells.

The Tannenbaum reference was characterized by the Applicant as described in the Draft Amendment. There was relatively little discussion between the Applicant and the Examiners regarding the Tannenbaum reference.

The Applicant explained his understanding that the Lanni reference was cited by the Examiner for the purpose of providing motivation to combine the Lee and Tannenbaum references, and believe that Examiner Yu confirmed that understanding and indicated that Lanni teaches combining at least two anti-tumor therapeutic methods. The Applicant pointed out that Lanni describes only a single method of killing tumor cells - namely, treating them with conditioned medium that is obtained from macrophages cultured in the presence of paclitaxel and that is optionally contacted with one of two antibodies prior to application of the conditioned medium to tumor cells. The Examiners were unable to indicate where Lanni disclosed combining anti-tumor treatments. The Applicants believe that the Examiners were unable to otherwise indicate how Lanni might be relevant to the claimed invention or how Lanni might motivate a skilled artisan to combine the Lee and Tannenbaum references.

The Applicant suggested that even if it could be assumed that a reference exists that teaches the apparent axiom that "two treatments are better than one," there is no reason to combine the Lee and Tannenbaum references. Lee teaches, at best, local administration of a particular antigen-releasing agent that renders the claimed method inoperative and does not teach that any therapeutic effect is obtained against non-engineered tumors (see open and filled circles in Figure 11 of Lee). Tannenbaum teaches that only IL-12 (a second IR1-promoting agent) exhibits anti-tumor activity. Thus, the Applicant pointed out, no combination of references cited by the Examiner teaches administration (local or otherwise) of a leukocyte attractant or IFN-g to a tumor in a human, and no reference or combination of references teaches combination therapy using the four agents recited in the claims for local administration to a tumor.

The enablement rejection of claims 2 and 4-6 was discussed only briefly. The Applicants indicated their understanding that the rejection was based on the Examiners' contention that administration of a protease to a tumor could lead to tumor growth, spread, or

metastasis. The Applicant pointed out that there was no evidence or reasoning presented on the record on which such a contention could be based, and that occurrence of tumor growth, spread, or metastasis was irrelevant to the claimed invention (which does not recite lack of tumor growth, spread, or metastasis).

Other Pertinent Matters Discussed

Examiner Yu raised an objection that the Applicant was unable to understand. To the best of the Applicant's understanding, the objection related to Examiner Yu's belief that either i) leukocytes beyond the site of locally-administered anti-Fas antibody (i.e., beyond the tumor site) could potentially be affected by anti-Fas antibody or ii) anti-Fas antibody locally administered to a tumor site might potentially kill fewer than all leukocytes at the tumor site. The Applicant expressed inability to understand the point that the Examiner was trying to make or the relevance of that point to the patentability of the claims. The Applicant did not receive a clarifying explanation of Examiner Yu's point from either of the other Examiners present. The Applicant pointed out that a skilled artisan would recognize that the claimed method involves activating a patient's T leukocytes to fight the patient's tumor, and that an agent (i.e., anti-Fas antibody) that kills substantial numbers of (Fas-bearing) activated T leukocytes would be inappropriate for use in the claimed methods, regardless of the possibility that a few activated T leukocytes would not be killed.

Near the close of the time allotted for the interview, the Applicant requested allowance of the claims, in view of the Applicant's belief that all of the Examiners' claim rejections had been convincingly overcome. The Examiners indicated that at least certain of the Applicant's arguments appeared to cast doubt upon the sustainability of the Examiners' rejections, and that further consideration of the Applicant's arguments would be undertaken upon formal submission of those arguments.

The Applicant protested, indicating their belief that the Examiners' rejections had been equally convincingly overcome multiple times in the past, and that the result of each subsequent post-interview reconsideration was essentially repetition of the same rejections

without any significant counterargument to the points raised by the Applicant. The Examiners replied that the Applicant's frustration was understood, and assured the Applicant that the Applicant's arguments would be given serious consideration during the 30-day period following their formal submission.

Outcome of the Interview

No agreement was reached regarding patentability of the pending claims. The Applicant agreed to formally submit the Applicant's arguments in the very near future, in view of the fact that the Examiners are no longer permitted to accept a formal paper during the interview.

This Summary is accurate to the best recollection of the undersigned Applicant's representative.

Respectfully submitted,

Eugene Roussel

11 June 2004
(Date)

By: _____

Gary D. Colby, Ph.D., J.D.
Registration No. 40,961
Customer No. 08933
DUANE MORRIS LLP
One Liberty Place
Philadelphia, PA 19103-7396
Telephone: 215-979-1000
Direct Dial: 215-979-1849
Facsimile: 215-979-1020
E-Mail: GDColby@DuaneMorris.com